



# Improved Nutritional Management of Phenylketonuria using the intact protein Glycomacropeptide compared with Amino Acids



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## Abstract

Glycomacropeptide (GMP), an intact whey protein formed as a by-product of cheese production, contains minimal phenylalanine (phe) and can be made into a variety of foods and beverages. To evaluate the safety and efficacy of replacing all amino acid (AA)-based formula with GMP food products, an 8-day inpatient metabolic study was completed with 11 subjects with PKU (age range 11.5 to 31 years). There were no medical concerns on the GMP diet and 10 of 11 subjects preferred the GMP diet to the AA diet. There was no significant difference in the phe concentration in postprandial plasma with the GMP diet compared with the AA diet. GMP improved phe and protein utilization as shown by reduced daily variation of phe concentrations in fasting and postprandial plasma, significantly lower postprandial blood urea nitrogen and higher insulin concentrations with the GMP diet compared with AA diet. GMP, when supplemented with limiting amino acids, is a safe and acceptable alternative to synthetic AA as the primary protein source in the nutritional management of PKU.

## Introduction

PKU requires life-long treatment with a low phe diet that provides the majority of protein from phe-free AA formula. Compliance with the PKU diet is difficult and new approaches to diet treatment are needed.

GMP is a 64-amino acid glycomacropeptide produced during cheese manufacturing. Pure GMP contains no aromatic AA, including phe (1). Various foods and beverages can be made with GMP to contain 5 to 12 g protein equivalents and 15 to 30 mg phe/serving. Blind sensory evaluations show that GMP products are well accepted by those with PKU (2).



**Study Objective:** To evaluate the efficacy of replacing all AA formula with GMP food products on acceptability, safety, plasma AA concentrations and measures of protein utilization in a controlled metabolic study (3).

## Methods

Eleven subjects with PKU, age range 11.5 to 31 years, participated in an 8-day inpatient metabolic study. All subjects entered the study with stable plasma phe concentrations ranging from 330 to 1010  $\mu\text{mol/L}$ .

The study included two 4-day diets:

**AA Diet** = Each subject's current diet with AA formula

**GMP Diet** = Formula was stopped and GMP products replaced all protein equivalents provided by the AA formula.

The GMP was supplemented with 5 amino acids that are limiting in this protein source: tyrosine, histidine, leucine, tryptophan and methionine.

The diets were matched in phe, energy and total protein (Table 1).

Analysis of 24-hour food composites confirmed that the phe content of both diets was not significantly different.

**Table 1: Example menus for AA Diet and GMP Diet**

AA formula		GMP Foods	
Dinner (220 mg phe, 18 g protein)		Dinner (220 mg phe, 18 g protein)	
Amount	Phe (mg)	Amount	Phe (mg)
177 mL PKU Formula	0 mg	1 GMP Bar	33 mg
		237 mL GMP sports beverage	19 mg
Pasta Alfredo:	113 mg	Pasta Alfredo:	61 mg
14 g regular pasta		5 g regular pasta	
60 g low pro pasta		60 g low pro pasta	
88 g low pro Alfredo sauce		88 g low pro Alfredo sauce	
92 g Broccoli	82 mg	92 g Broccoli	82 mg
50 g Carrots	18 mg	50 g Carrots	18 mg
140 g Pears	7 mg	140 g Pears	7 mg

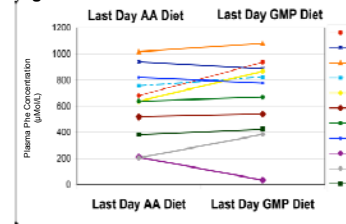
## Results

Ten of 11 subjects preferred the taste and other sensory qualities of the GMP Diet compared with AA Diet.

No adverse health effects were detected on physical exam. Albumin, prealbumin, IGF-1 and other blood chemistries remained normal with GMP compared with AA Diet.

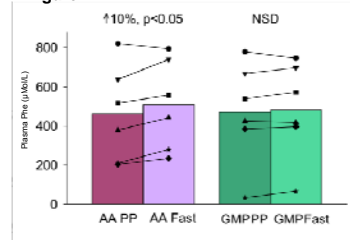
**Paired, mean plasma phe concentrations were not significantly different on GMP Diet compared with AA Diet (Figure 1).**

**Figure 1**



**As an intact protein source, GMP can improve protein utilization.** Various studies have shown that protein synthesis and nitrogen retention are greater with ingestion of intact protein compared with amino acids (4,5).

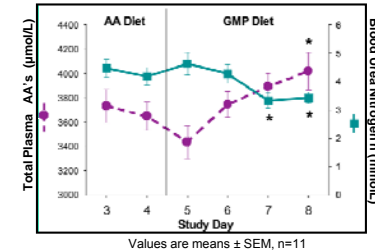
**Figure 2**



**When comparing fasting with postprandial (PP) plasma collected 2.5 hours after breakfast, fasting phe concentrations were significantly higher than PP concentrations with the AA Diet, but not with the GMP Diet (Figure 2).** This suggests that the GMP Diet induced less variation and potentially lower mean concentrations of phe over a 24-hour period.

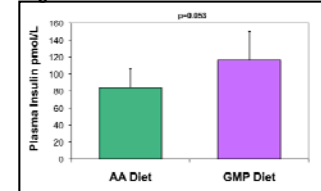
**In plasma collected 2.5 hours after breakfast, total amino acid concentrations were significantly greater and blood urea nitrogen (BUN) significantly lower on the GMP Diet compared with AA Diet (Figure 3).** This suggests slower absorption of amino acids and reduced ureagenesis with the intact protein GMP compared with amino acids.

**Figure 3**



Values are means  $\pm$  SEM, n=11

**Figure 4**



Values are Mean  $\pm$  SEM, n=11. Glucose levels were NSD

**Postprandial insulin concentration was higher on GMP Diet compared to AA Diet (Figure 4).** Since post-absorptive amino acids stimulate insulin release, higher insulin concentrations suggest improved protein synthesis and reduced amino acid degradation with the GMP Diet compared with AA Diet.

Evaluation of the plasma concentrations of the limiting amino acids added to the GMP suggest that arginine should be added, but additional methionine is not required.

## Conclusions

1. GMP, supplemented with limiting AA, appears to be a safe alternative to replace some, or all of the traditional synthetic amino acid-based formulas in the PKU diet.
2. As an intact protein, GMP improves phe and protein utilization compared with a synthetic amino acid source.
3. Foods and beverages made with GMP may provide a new diet option for those with PKU.

## References

1. Ney DM et al. J Inher Metab Dis 2009; 32: 32-39.
2. Lim K et al. Mol Genet Metab 2007; 92:176-178
3. Van Calcar SC et al. Am J Clin Nutr 2009; 89: 1068-77.
4. Metjes CC et al. Am J Physiol Endocrinol Metab 2000; 278:E1000-9.
5. Cropper SS, Acosta PB. J Parenteral Enteral Nutr 1991; 15:48-53.